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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1812	7

DATE MAILED: 01/21/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined FOR RESTRICTION ONLY ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 0 month(s), 30 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-79 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☐ Claims _____ are rejected.

5. ☐ Claims _____ are objected to.

6. ☑ Claims 1-79 are subject to restriction or election requirement.

7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Detailed Action

Claims 1-33, 66-79 are pending in the Instant Application

1. The election **without traverse** of Groups I and II, claims 1-33 and 66-79 filed 2/25/97 (paper No. 8) has been entered. Claims 34-65 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

2. The instant specification does not comply with 37 CFR § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Applicant should note that at least the following sequences require a sequence identifier:

pages 25 table IV, sequences 027-029; 031-033
page 28 table V, sequences 025-023
page 38 line 29

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-33, 66-79 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for the claims limited to the specific construction, expression and screening of antibody fragments on the surface of M13, and cloning of heavy and light chain sequences without restriction sequences (examples I and II).

Support for claims which as drafted use the phrases "comprising a plurality of cells containing diverse combinations of first and second DNA sequences encoding first and second polypeptides which form heteromeric receptors, one or both of said polypeptides being expressed as fusion proteins on the surface of a cell..." or "...the coexpression of two or more DNA sequences encoding polypeptides which form heteromeric receptors comprising two vectors..." or "...two or more DNA sequences encoding polypeptides which form a heteromeric receptor, comprising a set of first vectors having a diverse population of second DNA sequences..." is not commensurate with the scope of the claims. The specification is not commensurate with the breadth of the claims because as drafted the claims encompass any fragment/mutant/variant/deletion/substitution of an polypeptide which has the same biological activity as the disclosed antibody fragments and heavy and light chain sequences irrespective of sequence identity. In addition although the breadth of the instant claims embrace proteins of many multiple sequences with

less than 100% identity to that of the disclosed antibody fragments of example I and heavy and light chain sequences of example II, the simple fact that a two proteins share a large percentage of their encoded amino acids/nucleotides in no way supports the conclusion that they are in any way functionally analogous or can be made or used in the manner disclosed in the instant application.

Furthermore, the specification provides little guidance other than the disclosure of the antibody fragments (example I) and heavy and light chain sequences of example II. Because of this lack of guidance, the extended experimentation that would be required to determine which other fragments/substitutions/deletions/fusions/derivitizations or other variants would retain the desired binding properties/activities of the instantly claimed sequences, and because of the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at which of the as yet uncharacterized polypeptide variants or fragments have the desired binding/biological activities and properties. In addition, in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2D 1016 (Fed Cir. 1991), the court ruled that a claim to a large genus of possible sequences encoding a protein with a

particular function that needs to be determined subsequent to the construction of the sequences may not find sufficient support under 35 U.S.C. 112, first paragraph, if only a few of the compounds that meet the functional limitations of the claim(s) are disclosed and if undue experimentation would be required of one skilled in the art for the determination of other sequences that are embraced by the claim; the instant application is directly analogous. Hence, because it would require undue experimentation to identify which of the other uncharacterized sequences/structures have the aforementioned activities/properties, the entire scope of claims is not enabled. The aforementioned claims are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is only enabling for the claims limited to the disclosed antibody fragments and heavy and light chain sequences recited in Examples I and II.

4. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, and 16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. The claims as presently drafted use relative language (e.g. "...diverse...") which does not have a single or unambiguous art-accepted meaning, making it unclear what Applicant intends to claim as the instant invention. Claims 2-8, and 76-78, and 17-25 are rejected as indefinite in so far as they depend from claim 1.

Claim 4-5, 19-20, 39-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims as presently drafted use confusing language (e.g. "...functional portions...") making it unclear what Applicant intends to claim as the instant invention.

Claims 9-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 uses the language "...useful..." which is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This term is vague and indefinite because this term is relative and it is unclear if the applicant intends to describe the kit with a qualifier or if useful is intended to connote some other aspect for the expression as outlined, hence it is unclear what applicant intends or what

specifically claims reciting this language include or exclude rendering such claims uninterpretable.

Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim as presently drafted uses indefinite language having no antecedent basis (e.g. "expression polypeptides").

Claim 5 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim as presently drafted uses confusing language (e.g. "...cloning site for containing...") making it unclear what Applicant intends to claim as the instant invention.

Claims 6-8, 22-24, 26 and 31-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 6-8, 22-24 and 31-33 are confusing because they do not indicate that there is any functional relationship between the recited bacteriophage and the cells producing them. Claim 26 is confusing for the term "possible" and for effectively claiming a plurality of polypeptides forming a single receptor which binds a single molecule and in its "operable" linkages to genes. Claims 27-33

and 79 are rejected in so far as they depend from the aforementioned rejected claims.

Claim 66-67, 70, 71-72 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims as presently drafted use relative language (e.g. "...capable of..." or "...substantially...") which do not have a single or unambiguous art-accepted meaning, making it unclear what Applicant intends to claim as the instant invention.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9, 16, 66 and 71 are rejected under 35 U.S.C. § 102**(a)** as being anticipated by Huse et al. 1989 (Applicants reference). As drafted claims 9-15 are directed to vectors for the coexpression of two or more DNA sequences encoding

polypeptides which form heteromeric receptors comprising two vectors, wherein one or both vectors contains sequences necessary for expression of polypeptides encoded by DNA sequences inserted in cloning sites and further limited in that said vectors are circular, said expression peptides are fusion proteins on the surface of cells, wherein said cell produces filamentous bacteriophage and wherein said filamentous bacteriophage is selected from the group consisting of M13, fd and f1, limitations which are taught by Huse et al. 1989 (see abstract, Figures 1-8, tables 1-2 and pages 1276-1280).

Claims 1, 9, 16, 26, 66 and 71 are rejected under 35 U.S.C. § 102**(b)** as being anticipated by either of Parmley and Smith (1988 and 1989, Applicants references). As drafted claims 9-15 are directed to vectors for the coexpression of two or more DNA sequences encoding polypeptides which form heteromeric receptors comprising two vectors, wherein one or both vectors contains sequences necessary for expression of polypeptides encoded by DNA sequences inserted in cloning sites and further limited in that said vectors are circular, said expression peptides are fusion proteins on the surface of cells, wherein said cell produces filamentous bacteriophage and wherein said filamentous bacteriophage is selected from the group consisting of M13, fd and f1, limitations which are taught by either of Parmley and Smith 1988 and 1989 (in Parmley and Smith 1988, see abstract,

Figure 1 and pages 215-218; in Parmley and Smith 1989, see abstract, Figures 1-2, tables 1-2 and pages 306-316).

6. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-5, 16-21 and 25-30, 66 and 71 are rejected under 35 U.S.C. § 103 as being unpatentable over Huse et al. 1989 in view of the Ladner patent WO8806630 (both Applicants references).

The subject of these claims differs from the cells, vectors and cloning system disclosed in the Huse reference in having the receptor protein of the instant invention expressed on the surface of a host cells as opposed to that disclosed in the huse reference which is confined to the host cell cytoplasm. The Ladner reference teaches that the expression of an antibody

derived binding protein on the surface of a recombinant host organism to allow for the identification of those host organisms carrying DNA sequences encoding binding proteins with the desired binding characteristics was fairly taught in the art prior to the making of the instant invention. To use a surface expression system like the one described in the Ladner patent in a binding protein generating system like that disclosed in the Huse et al. reference to reduce the effort required to identify a host organism carrying a DNA sequence encoding a protein having the desired binding characteristics would have been obvious to one of ordinary skill in the art at the time of the instant invention.

Claims 6-8, 22-24 and 31-33 and 66-79 are rejected under 35 U.S.C. § 103 as being unpatentable over the Huse et al. and Ladner patent WO8806630 (Applicants references) as applied to claims 1-5, 16-21 and 25-30 above and further in view of the Parmley and Smith 1988 (Applicants reference) publication. These claims further limit those above to the use of a filamentous bacteriophage vector which as shown in the Parmley and Smith reference, were used routinely in the art prior to the instant invention.

Claims 1-5, 16-21, 25-30 and 66-79 are rejected under 35 U.S.C. § 103 as being unpatentable over Sastry et al. (Applicants reference) in view of the Ladner WO8806630 and Robinson WO8702671 patents (Applicants references). The Sastry et al. reference

describes the instant invention in its entirety (see pages 5728-5731) but does not describe its complete reduction to practice; the Ladner and Robinson patents teach that he methods needed to reduce the system taught by Sastry et al. to practice were well known in the art prior to the publication of Sastry et al. and prior to the instant invention. To completely reduce the system taught by Sastry et al. to practice through the use of conventional method like those taught in the Ladner and Robinson patents would have been obvious to one of ordinary skill in the art at the time that the instant invention was made. Explicit motivation to use all of the aforementioned references can be found in the entire abstract of Parmley and Smith 1989 which states that one of ordinary skill in the art would be motivated to use these methods to "study eptitopes on immunologically important proteins without the use of synthetic peptides and without having ever cloned the genes".

Thus the claimed invention as a whole was *prima facie* obvious over the prior art.

7. Cited as art of interest are references listed on FORM PTO-892

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth A. Sorensen at telephone number (703) 305-5377. The examiner can

normally be reached on Monday through Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh can be reached on (703) 308-2957. The FAX phone number for this group is (703)308-0294.

Any inquiry of general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Kenneth A. Sorensen
Examiner
Group 1800

JOHN ULM
PRIMARY EXAMINER
GROUP 1800